Patent Claims

1. Compounds of formula 1

in which

R1 is hydroxyl, 1-4C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, 2,2-difluoroethoxy, or completely or predominantly fluorine-substituted 1-4C-alkoxy,

R2 is hydroxyl, 1-4C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, 2,2-difluoroethoxy, or completely or predominantly fluorine-substituted 1-4C-alkoxy,

or in which

R1 and R2 together are a 1-2C-alkylenedioxy group,

R3 is hydrogen or 1-4C-alkyl,

R31 is hydrogen or 1-4C-alkyl,

either, in a first embodiment (embodiment a) according to the present invention,

R4 is -O-R41, in which

R41 is hydrogen, 1-4C-alkyl, completely or predominantly fluorine-substituted 1-4C-alkyl, 1-4C-alkyl-1-4C-alkyl, hydroxy-2-4C-alkyl or 1-7C-alkylcarbonyl, and

R5 is hydrogen or 1-4C-alkyl,

or, in a second embodiment (embodiment b) according to the present invention,

R4 is hydrogen or 1-4C-alkyl, and

R5 is -O-R51, in which

R51 is hydrogen, 1-4C-alkyl, completely or predominantly fluorine-substituted 1-4C-alkyl, 1-4C-alkyl-1-4C-alkyl, hydroxy-2-4C-alkyl or 1-7C-alkylcarbonyl,

R6 is hydrogen, halogen, nitro, 1-4C-alkyl, trifluoromethyl or 1-4C-alkoxy,

R7 is a radical of formulae (a), (b), (c) or (d)

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in which

if R7 is a radical of the formula (b),

either

R8, R9, R10 and R11 independently of one another are hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl, 3-7C-cycloalkylmethyl, cyano, hydroxy-2-4C-alkyl, 1-4C-alkoxy-2-4C-alkyl or R28,

or

R8 is hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl, 3-7C-cycloalkylmethyl, hydroxy-2-4C-alkyl, 1-4C-alkoxy-2-4C-alkyl or R28,

R9 is is hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl, 3-7C-cycloalkylmethyl, hydroxy-2-4C-alkyl, 1-4C-alkoxy-2-4C-alkyl or R28, and

R10 and R11, together and including the nitrogen atom to which both are bonded, are a pyrrolidin-1-yl, piperidin-1-yl, azepan-1-yl, aze

or

R8 is hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl, 3-7C-cycloalkylmethyl, hydroxy-2-4C-alkyl, 1-4C-alkoxy-2-4C-alkyl or R28,

R9 is hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl, 3-7C-cycloalkylmethyl, hydroxy-2-4C-alkyl, 1-4C-alkoxy-2-4C-alkyl or R28,

R10 is hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl, 3-7C-cycloalkylmethyl, hydroxy-2-4C-alkyl, 1-4C-alkoxy-2-4C-alkyl or R28, and

R11 is Aryl1, naphthyl, phenyl, phenyl substituted by R20 and/or R21, phenyl-1-4C-alkyl or phenyl-1-4C-alkyl substituted by R22 and R23,

in which

if R7 is a radical of the formula (c),

either

R12, R13, R14 and R15 independently of one another are hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl methyl, hydroxy-2-4C-alkyl, 1-4C-alkoxy-2-4C-alkyl or R28,

or

R12 and R13 independently of one another are hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl, 3-7C-cycloalkylmethyl, hydroxy-2-4C-alkyl, 1-4C-alkoxy-2-4C-alkyl or R28, and R14 and R15, together and including the nitrogen atom to which both are bonded, are a pyrrolidin-1-yl, piperidin-1-yl, azepan-1-yl, azocan-1-yl, azonan-1-yl, azecan-1-yl, morpholin-4-yl, tetrahydroisoquinolin-2-yl, tetrahydro-6,7-dimethoxyisoquinolin-2-yl, 3,5-dimethyl-pyrazol-1-yl, pyrazol-1-yl, 2,6-dimethyl-morpholin-4-yl, 2,6-dimethyl-piperidin-1-yl, 4-benzyl-piperidin-1-yl, thiomorpholin-4-yl or 1H-1,2,4-triazol-1-yl radical, or a piperazin-1-yl radical substituted in 4-position by R19,

or

R12 and R13, together and including the nitrogen atom to which both are bonded, are a pyrroli-din-1-yl, piperidin-1-yl, azepan-1-yl, morpholino-4-yl, 4-(1-4C-alkyl-)-piperazin-1-yl, 2,6-di-methyl-morpholin-4-yl, 2,6-dimethyl-piperidin-1-yl, 4-benzyl-piperidin-1-yl or thiomorpholin-4-yl radical, and

R14 and R15, together and including the nitrogen atom to which both are bonded, are a pyrrolidin-1-yl, piperidin-1-yl, azepan-1-yl, morpholino-4-yl, 4-(1-4C-alkyl-)-piperazin-1-yl, 2,6-dimethyl-morpholin-4-yl, 2,6-dimethyl-piperidin-1-yl, 4-benzyl-piperidin-1-yl or thiomorpholin-4-yl radical,

or

R12 and R15 independently of one another are hydrogen or 1-4C-alkyl, and R13 and R14, together and with inclusion of the N-C(=)-N structure to which they are bonded, are a hexahydropyrimidin-2-ylidene or imidazolidin-2-ylidene radical,

in which

if R7 is a radical of the formula (d),

R16 is hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl, 3-7C-cycloalkylmethyl, hydroxy-2-4C-alkyl, 1-4C-alkoxy-2-4C-alkyl or R28, and

R17 and R18, together and with inclusion of the N-C(-)-N structure to which they are bonded are Aryl2,

- Aryl1 is 4-methylthiazol-2-yl, benzimidazol-2-yl, 5-nitrobenzimidazol-2-yl, 5-chlorobenzimidazol-2-yl, 5-methylbenzimidazol-2-yl, 4-methylquinazolin-2-yl, benzothiazol-2-yl, benzoxazol-2-yl or pyrimidin-2-yl,
- Aryl2 is 1-methyl-4-oxo-4,5-dihydro-1H-imidazol-2-yl, imidazol-2-yl, 4,5-dicyano-imidazol-2-yl, 4-methyl-imidazol-2-yl, 4-ethyl-benzimidazol-2-yl, 4-acetyl-imidazol-2-yl, 1H-[1,2,4]triazol-3-yl, benzimidazol-2-yl, 1-methyl-benzimidazol-2-yl, 1-ethyl-benzimidazol-2-yl, 5,6-dimethyl-benzimidazol-2-yl, purin-8-yl, 6-amino-7-methyl-7H-purine-8-yl, 1,6-dimethylimidazo[4,5-b]pyridin-2-yl, 1,5,6-trimethylimidazo[4,5-b]pyridin-2-yl, 1,3-dimethyl-3,7-dihydro-1H-purine-2,6-dione-8-yl, 7-ethyl-3-methyl-3,7-dihydro-purine-2,6-dione-8-yl, 1,3,7-trimethyl-3,7-dihydro-purine-2,6-dione-8-yl, thiadiazolyl, 1,4-dihydrotetrazol-5-yl, 1H-[1,2,4]triazol-3-yl, 1,3-dihydrobenzimidazol-5-yl, 1H-tetrazol-5-yl, pyrimidin-2-yl or 4,6-dimethyl-pyrimidin-2-yl,

- R19 is 1-4C-alkyl, formyl, 3-7C-cycloalkyl, 3-7C-cycloalkylmethyl, 1-4C-alkoxycarbonyl-1-4C-alkyl, 1-4C-alkoxy-2-4C-alkyl, hydroxy-2-4C-alkoxy-2-4C-alkoxy-2-4C-alkoxy-2-4C-alkoxy-2-4C-alkoxy-2-4C-alkoxy-2-4C-alkyl, phenyl, phenyl substituted by R24 and/or R25, [benzo(1,3)dioxol]-5-ylmethyl, phenyl-1-4C-alkyl or phenyl-1-4C-alkyl substituted in the phenyl moiety by R26 and/or R27,
- R20 is halogen, nitro, carboxyl, 1-4C-alkyl, trifluoromethyl or 1-4C-alkoxy,
- R21 is halogen, 1-4C-alkyl or 1-4C-alkoxy.
- R22 is halogen, nitro, carboxyl, 1-4C-alkyl, trifluoromethyl or 1-4C-alkoxy,
- R23 is halogen, 1-4C-alkyl or 1-4C-alkoxy.
- R24 is halogen, nitro, carboxyl, 1-4C-alkyl, 1-4C-alkylcarbonyl, trifluoromethyl or 1-4C-alkoxy,
- R25 is halogen, 1-4C-alkyl or 1-4C-alkoxy,
- R26 is halogen, nitro, carboxyl, 1-4C-alkyl, trifluoromethyl or 1-4C-alkoxy,
- R27 is halogen, 1-4C-alkyl or 1-4C-alkoxy,
- R28 is R29(R30)N-2-4C-alkyl wherein
- R29 and R30, together and including the nitrogen atom to which both are bonded, are a pyrrolidin-1-yl, piperidin-1-yl, piperazin-1-yl, 4-(1-4C-alkyl-)piperazin-1-yl, azepan-1yl, azecan-1-yl, azecan-1-yl, tetrahydroisoquinolin-2-yl, tetrahydro-6,7-dimethoxyisoquinolin-2-yl, 3,5-dimethyl-pyrazol-1-yl, pyrazol-1-yl, morpholin-4-yl, 2,6-dimethyl-morpholin-4-yl, 2,6-dimethyl-piperidin-1-yl, 4-benzyl-piperidin-1-yl, thiomorpholin-4-yl or 1H-1,2,4-triazol-1-yl radical, the salts of these compounds, as well as the N-oxides, enantiomers, E/Z isomers and tautomers of these compounds and their salts.
- 2. Compounds of formula 1 according to claim 1 in which
- R1 is 1-2C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, 2,2-difluoroethoxy, or completely or predominantly fluorine-substituted 1-2C-alkoxy,
- R2 is 1-2C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, 2,2-difluoroethoxy, or completely or predominantly fluorine-substituted 1-2C-alkoxy.
- R3 is hydrogen,
- R31 is hydrogen,

either, in a first embodiment (embodiment a) according to the present invention,

- R4 is -O-R41, in which
- R41 is hydrogen or 1-4C-alkylcarbonyl, and
- R5 is hvdragen.
- or, in a second embodiment (embodiment b) according to the present invention,
- R4 is hydrogen, and
- R5 is -O-R51, in which
- R51 is hydrogen or 1-4C-alkylcarbonyl,
- R6 is hydrogen, halogen, nitro, 1-4C-alkyl, trifluoromethyl or 1-4C-alkoxy,
- R7 is a radical of formulae (a), (b), (c) or (d)

in which

if R7 is a radical of the formula (b),

either

R8 is hydrogen, and

R9, R10 and R11 independently of one another are hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

or

R8 is hydrogen,

R9 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl, and R10 and R11, together and including the nitrogen atom to which both are bonded, are a pyrroli-din-1-yl, piperidin-1-yl, azepan-1-yl, azocan-1-yl, azocan-1-yl, azecan-1-yl, morpholin-4-yl, tetrahydroisoquinolin-2-yl, 3,5-dimethyl-pyrazol-1-yl, pyrazol-1-yl, 2,6-dimethyl-morpholin-4-yl or 2,6-dimethyl-piperidin-1-yl radical, or a piperazin-1-yl radical substituted in 4-position by R19,

or

R8 is hydrogen,

R9 is hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl, R10 is hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl, and R11 is Aryl1, naphthyl, phenyl, phenyl substituted by R20 and/or R21, phenyl-1-4C-alkyl or phenyl-1-4C-alkyl substituted by R22 and R23,

in which

if R7 is a radical of the formula (c),

either

R12, R13, R14 and R15 independently of one another are hydrogen, 1-4C-alkyl, 3-7C-cyclo-alkyl or 3-7C-cycloalkylmethyl,

or

R12 and R13 independently of one another are hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl, and

R14 and R15, together and including the nitrogen atom to which both are bonded, are a pyrroli-din-1-yl, piperidin-1-yl, azepan-1-yl, az

or 2,6-dimethyl-piperidin-1-yl radical, or a piperazin-1-yl radical substituted in 4-position by R19,

or

R12 and R13, together and including the nitrogen atom to which both are bonded, are a pyrrolidin-1-yl, piperidin-1-yl, azepan-1-yl, morpholino-4-yl, 4-(1-4C-alkyl-)-piperazin-1-yl, 2,6-dimethyl-morpholin-4-yl or 2,6-dimethyl-piperidin-1-yl radical, and R15, together and including the nitrogen atom to which both are bonded, are a pyrrolidin-1-yl, piperidin-1-yl, azepan-1-yl, morpholino-4-yl, 4-(1-4C-alkyl-)-piperazin-1-yl, 2,6-dimethyl-morpholin-4-yl or 2,6-dimethyl-piperidin-1-yl radical,

or

R12 and R15 independently of one another are hydrogen or 1-4C-alkyl, and R13 and R14, together and with inclusion of the N-C(=)-N structure to which they are bonded, are a hexahydropyrimidin-2-ylidene or imidazolidin-2-ylidene radical,

in which

if R7 is a radical of the formula (d).

R16 is hydrogen, and

R17 and R18, together and with inclusion of the N-C(-)-N structure to which they are bonded are Aryl2,

- Aryl1 is 4-methylthiazol-2-yl, benzimidazol-2-yl, 5-nitrobenzimidazol-2-yl, 5-chlorobenzimidazol-2-yl, 5-methylbenzimidazol-2-yl, benzothiazol-2-yl or benzoxazol-2-yl,
- Aryl2 is 1-methyl-4-oxo-4,5-dihydro-1H-imidazol-2-yl, imidazol-2-yl, 4,5-dicyano-imidazol-2-yl, 4-methyl-imidazol-2-yl, 4-ethyl-benzimidazol-2-yl, 4-acetyl-imidazol-2-yl, 1H-[1,2,4]triazol-3-yl, benz-imidazol-2-yl, 1-methyl-benzimidazol-2-yl, 1-ethyl-benzimidazol-2-yl, 5,6-dimethyl-benzimidazol-2-yl, purin-8-yl, 6-amino-7-methyl-7H-purine-8-yl, 1,6-dimethylimidazo[4,5-b]pyridin-2-yl, 1,5,6-trimethylimidazo[4,5-b]pyridin-2-yl, 1,3-dimethyl-3,7-dihydro-1H-purine-2,6-dione-8-yl, 7-ethyl-3-methyl-3,7-dihydro-purine-2,6-dione-8-yl, 1,3,7-trimethyl-3,7-dihydro-purine-2,6-dione-8-yl or 1H-[1,2,4]triazol-3-yl,
- R19 is 1-4C-alkyl, formyl, 1-4C-alkylcarbonyl, 2-hydroxyethyl, phenyl, phenyl substituted by R24 and/or R25, phenyl-1-4C-alkyl or phenyl-1-4C-alkyl substituted in the phenyl moiety by R26 and/or R27,
- R20 is halogen, nitro, 1-4C-alkyl or 1-4C-alkoxy,
- R21 is halogen, 1-4C-alkyl or 1-4C-alkoxy.
- R22 is halogen, nitro, 1-4C-alkyl or 1-4C-alkoxy.
- R23 is halogen, 1-4C-alkyl or 1-4C-alkoxy,
- R24 is halogen, nitro, carboxyl, 1-4C-alkyl or 1-4C-alkoxy,
- R25 is halogen, 1-4C-alkyl or 1-4C-alkoxy,
- R26 is halogen, nitro, 1-4C-alkyl or 1-4C-alkoxy.
- R27 is halogen, 1-4C-alkyl or 1-4C-alkoxy.

the salts of these compounds, as well as the N-oxides, enantiomers, E/Z isomers and tautomers of these compounds and their salts.

3. Compounds of formula 1 according to claim 1 in which

R1 is 1-2C-alkoxy, 2,2-difluoroethoxy, or completely or predominantly fluorine-substituted 1-2C-alkoxy,

R2 is 1-2C-alkoxy, 2,2-difluoroethoxy, or completely or predominantly fluorine-substituted 1-2C-alkoxy,

R3 is hydrogen,

R31 is hydrogen,

either, in a first embodiment (embodiment a) according to the present invention,

R4 is -O-R41, in which

R41 is hydrogen or 1-4C-alkylcarbonyl, and

R5 is hydrogen,

or, in a second embodiment (embodiment b) according to the present invention,

R4 is hydrogen, and

R5 is -O-R51, in which

R51 is hydrogen or 1-4C-alkylcarbonyl,

R6 is hydrogen,

R7 is a radical selected from

the salts of these compounds, as well as the N-oxides, enantiomers, E/Z isomers and tautomers of these compounds and their salts.

4. Compounds of formula 1 according to claim 1 in which

R1 is 1-2C-alkoxy, or completely or predominantly fluorine-substituted 1-2C-alkoxy,

R2 is 1-2C-alkoxy, or predominantly fluorine-substituted 1-2C-alkoxy,

R3 is hydrogen,

R31 is hydrogen,

R4 is -O-R41, in which

R41 is hydrogen or 1-4C-alkylcarbonyl, and

R5 is hydrogen,

R6 is hydrogen,

R7 is a radical of formula (c)

in which

either

R12 is hydrogen,

R13 is hydrogen,

R14 is hydrogen or 1-4C-alkyl, and

R15 is 1-4C-alkyl or 3-7C-cycloalkyl,

or

R12 is hydrogen,

R13 is hydrogen, and

R14 and R15, together and including the nitrogen atom to which both are bonded, are a pyrrolidin-1-yl, piperidin-1-yl, azepan-1-yl, azocan-1-yl, azocan-1-yl or morpholin-4-yl, radical, or a piperazin-1-yl radical substituted in 4-position by R19, in which

R19 is 1-4C-alkylcarbonyl,

the salts of these compounds, as well as the N-oxides, enantiomers, E/Z isomers and tautomers of these compounds and their salts.

5. Compounds of formula 1 according to claim 1 in which

R1 is methoxy, or ethoxy,

R2 is methoxy, ethoxy, 2,2-difluoroethoxy, or difluoromethoxy,

R3 is hydrogen,

R31 is hydrogen,

R4 is -O-R41, in which

R41 is hydrogen, and

R5 is hydrogen,

R6 is hydrogen,

R7 is bonded to the meta or para position with respect to the binding position in which the phenyl ring is bonded to the phenanthridine ring system, and is a radical of formula (c)

in which

either

R12 is hydrogen,

R13 is hydrogen,

R14 is 1-4C-alkyl, such as e.g. 1-2C-alkyl, and

R15 is 1-4C-alkyl, such as e.g. 1-2C-alkyl,

or

R12 is hydrogen,

R13 is hydrogen,

R14 is hydrogen, and

R15 is 3-5C-cycloalkyl, such as e.g. cyclopropyl,

or

R12 is hydrogen,

R13 is hydrogen, and

R14 and R15, together and including the nitrogen atom to which both are bonded, are a pyrrolidin-1-yl, piperidin-1-yl, azepan-1-yl, azocan-1-yl, azonan-1-yl or morpholin-4-yl radical, or a piperazin-1-yl radical substituted in 4-position by R19, in which

R19 is 1-4C-alkylcarbonyl,

the salts of these compounds, as well as the N-oxides, enantiomers, E/Z isomers and tautomers of these compounds and their salts.

6. Compounds of formula 1 according to claim 1 in which

R1 is methoxy,

R2 is methoxy, ethoxy, difluoromethoxy, or 2,2-difluoroethoxy,

R3 is hydrogen,

R31 is hydrogen,

R4 is -O-R41, in which

R41 is hydrogen, and

R5 is hydrogen,

R6 is hydrogen,

R7 is bonded to the meta or para position with respect to the binding position in which the phenyl ring is bonded to the phenanthridine ring system, and is a radical of formula (c)

in which

either

R12 is hydrogen,

R13 is hydrogen,

R14 is ethyl, and

R15 is ethyl,

or

R12 is hydrogen,

R13 is hydrogen,

R14 is hydrogen, and

R15 is cyclopropyl,

or

R12 is hydrogen,

R13 is hydrogen, and

R14 and R15, together and including the nitrogen atom to which both are bonded, are an azocan-1-yl radical, or a piperazin-1-yl radical substituted in 4-position by R19, in which

R19 is acetyl,

the salts of these compounds, as well as the N-oxides, enantiomers, E/Z isomers and tautomers of these compounds and their salts.

- 7. Compounds of formula 1 according to claim 1 selected from
- 1. N'-(1-{4-[(2RS,4aRS,10bRS)-9-(1,1-Difluoro-methoxy)-2-hydroxy-8-methoxy-1,2,3,4,4a,10b-hexahydro-phenanthridin-6-yl]-phenyl}-methanoyl)-N,N-diethyl-guanidine
- 2. N-(1-Amino-1-azocan-1-yl-methylene)-4-[(2RS,4aRS,10bRS)-9-(1,1-difluoro-methoxy)-2-hydroxy-8-methoxy-1,2,3,4,4a,10b-hexahydro-phenanthridin-6-yl]-benzamide
- 3. N-Cyclopropyl-N'-(1-{4-[(2RS,4aRS,10bRS)-9-(1,1-difluoro-methoxy)-2-hydroxy-8-methoxy-1,2,3,4,4a,10b-hexahydro-phenanthridin-6-yl]-phenyl}-methanoyl)-guanidine
- 4. N-[1-(4-Acetyl-piperazin-1-yl)-1-amino-methylene]-4-((2RS,4aRS,10bRS)-2-hydroxy-8,9-dimethoxy-1,2,3,4,4a,10b-hexahydro-phenanthridin-6-yl)-benzamide
- 5. N,N-Diethyl-N'-{1-[4-((2RS,4aRS,10bRS)-2-hydroxy-8,9-dimethoxy-1,2,3,4,4a,10b-hexahydro-phenanthridin-6-yl)-phenyl]-methanoyl}-guanidine and
- 6. N-(1-Amino-1-azocan-1-yl-methylene)-4-((2RS,4aRS,10bRS)-2-hydroxy-8,9-dimethoxy-1,2,3,4,4a,10b-hexahydro-phenanthridin-6-yl)-benzamide, the salts of these compounds, as well as the N-oxides, enantiomers, E/Z isomers and tautomers of these compounds and their salts.
- 8. Compounds of formula 1 according to any of the preceding claims, which have with respect to the positions 4a and 10b the configuration shown in formula 1*:

the salts of these compounds, as well as the N-oxides, enantiomers, E/Z isomers and tautomers of these compounds and their salts.

9. Compounds of formula 1 according to any of the preceding claims, which have with respect to the positions 2, 4a and 10b, or, respectively, 3, 4a and 10b the configuration shown either in formula 1a***** or in formula 1b*****:

the salts of these compounds, as well as the N-oxides, E/Z isomers and tautomers of these compounds and their salts.

- 10. Compounds of the formula 1 according to claim 1 for use in the treatment of diseases.
- 11. A pharmaceutical composition comprising one or more compounds of formula 1 according to claim 1 together with customary pharmaceutical excipients, diluents and/or vehicles.
- 12. The use of compounds of formula 1 according to claim 1 for the production of pharmaceutical compositions for treating respiratory disorders.
- 13. A method for treating illnesses in a patient comprising administering to said patient a therapeutically effective amount of a compound of formula 1 as claimed in claim 1.
- 14. A method for treating airway disorders in a patient comprising administering to said patient a therapeutically effective amount of a compound of formula 1 as claimed in claim 1.